



ADVANCED NEUROIMAGING IN CONCUSSION: A TRANSLATIONAL COLLABORATION OPPORTUNITY

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FINANCIAL DISCLOSURES

- None
- Unpaid consultant
 - IOC workgroup on psychiatric aspects of sports concussion
 - CDC Safety in Youth Sports, concussion group
 - Co-director, ENIGMA Sports Concussion Section
 - NCAA/ PAC 12 concussion research review panel

LEARNING OBJECTIVES:

AT THE CONCLUSION OF THIS PRESENTATION THE LEARNER WILL BE ABLE TO;

- Compare and contrast TBI and Concussion
- Discuss the role of biomarkers, specifically neuroimaging in concussion assessment and management
- List the challenges and opportunities for future research and collaboration in concussion neuroimaging

TBI VS CONCUSSION

- Kissing cousins, not identical twins
- Baron *Sunburn Analogy*
- Sensitization kindling model
 - Post et al
- Different role of neuroimaging
 - White matter vs grey matter impact

ROLE OF BIOMARKERS

- Despite ongoing research in imaging and proteomics
 - GFAP, NFL, SB100, UCH-L1 (and others)
 - DTI, NIS
 - Balance
 - Eye-tracking
- *No approved, FDA endorsed Biomarkers for Concussion*

NEED FOR LARGE INTERPROFESSIONAL COLLABORATIONS

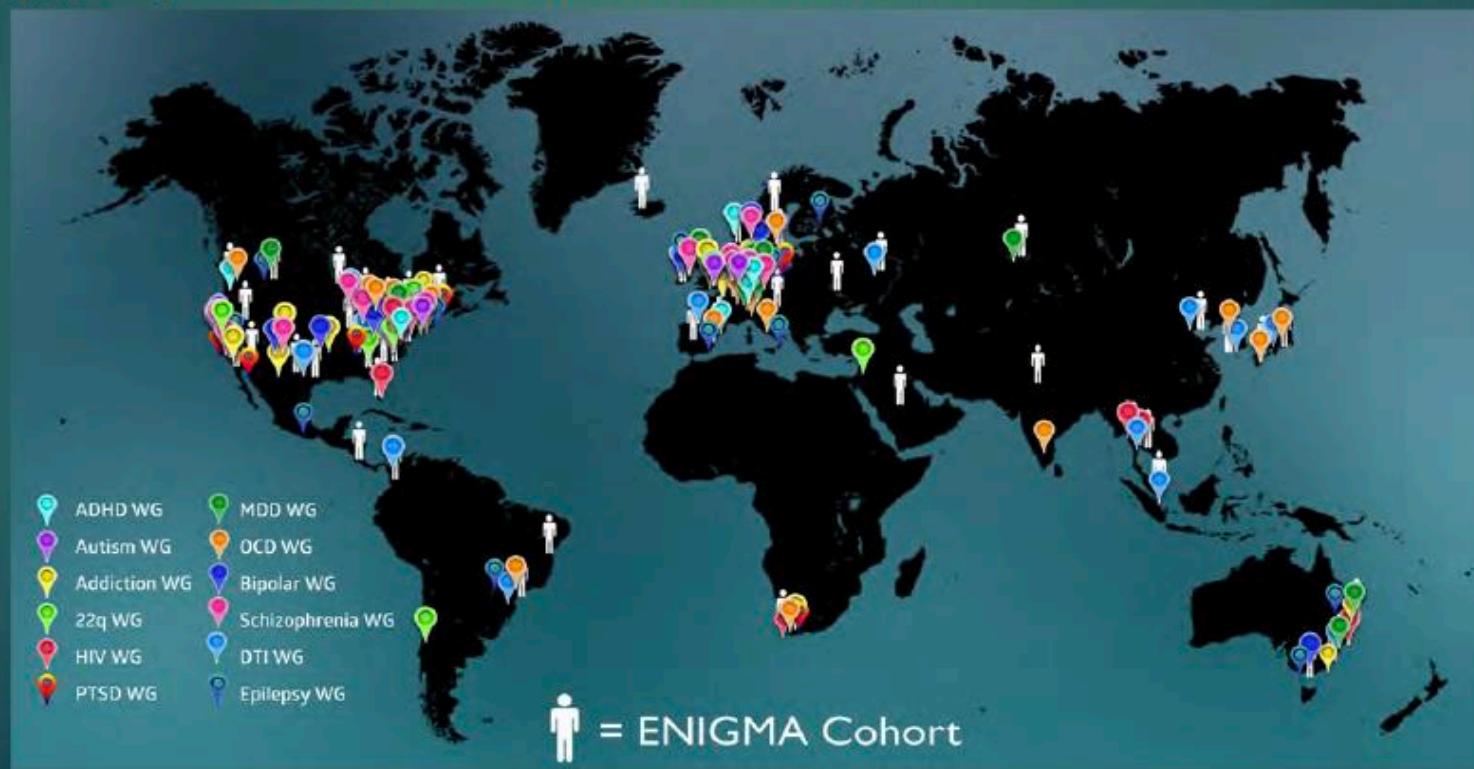
- Puzzle with many pieces
 - Need for translational approach- *Molecules to Mainstreet*
 - *Basic neuroscience/neuroimaging/neurogenetics*
 - *Clinical perspective*
 - *Public health/public policy*
 - *Osteopathic approach*

EXAMPLE OF COLLABORATION

- ENIGMA
- NHSCA-ISSP
- NCAA-IOC-FIFA

ENIGMA

- ▶ Started in 2009 – increased power for GWAS with brain measures
 - ▶ Brain measures as intermediate phenotype between genetics and psychiatric and neurological disorders
- ▶ 28+ working groups dedicated to psychiatric, neurological, and developmental disorders
 - ▶ Working groups dedicated to methods as well



ENIGMA Brain Injury

- ▶ Working group PIs: Emily Dennis (USC), David Tate (UMSL), Elisabeth Wilde (Utah)
- ▶ 38 groups across 9 countries so far
- ▶ ENIGMA Military Brain Injury
 - ▶ David Tate (UMSL) & Elisabeth Wilde (Utah)
- ▶ ENIGMA Pediatric msTBI
 - ▶ Emily Dennis (USC), Karen Caeyenberghs (ACU), Elisabeth Wilde (Utah)
- ▶ ENIGMA Sports Concussion
 - ▶ David Baron (USC) & Inga Koerte (Harvard and LMU)
- ▶ ENIGMA Adult msTBI
 - ▶ Alexander Olsen (NTNU) & Frank Hillary (Penn State)
- ▶ ENIGMA ED Civilian mTBI
 - ▶ Pratik Mukherjee (UCSF) & Andrew Mayer (UNM)
- ▶ ENIGMA Intimate Partner Violence
 - ▶ Carrie Esopenko (Rutgers)

ENIGMA Sports

- ▶ 3 sites
 - ▶ Total: n=54 Repetitive Head Impacts (RHI); n=13 Controls
- ▶ Diffusion MRI
- ▶ Results in RHI compared to controls
 - ▶ **Lower FA** in fronto-occipital fasciculus and borderline lower FA in the tapetum.
 - ▶ Borderline **higher MD** in the posterior thalamic radiation and tapetum
 - ▶ **Higher RD** in the tapetum, borderline higher RD in the superior fronto-occipital fasciculus
 - ▶ **Higher AD** in RHI in the corona radiata.

ENIGMA Sports

Poster tomorrow:
PS2.04.174



ENIGMA Sports-Related Brain Injury: Framework and Preliminary dMRI Meta-analysis



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Introduction

athletes participating in contact sports are exposed to repetitive head impacts (RHI), evidence suggests a link between RHI and impaired cognitive function in adolescents and young adults, but the underlying pathophysiology remains to be elucidated. Diffusion MRI (dMRI) is highly sensitive, but imaging studies investigating RHI are generally small and results are mixed. Here, we used the meta-analytic approach of the ENIGMA Consortium to analyze the effects of RHI on white matter microstructure across multiple cohorts.

Methods

was processed with a harmonized protocol based on "BSE event-based spatial statistics" (BSE-EBSS; www.bse-ebss.com). Prevalence (PA), year diffusivity (MD), space diffusivity (SD), and spatial diffusivity (AD) were calculated, and averaged across the ENIGMA dataset, and within each of 5 million, and 25 bilaterally averaged white matter (WM) regions of interest (ROI) from the study. To keep inter-variable (HU) bias, RHE/contro effect sizes were calculated within each site. Statistical results were then pooled across sites to conduct a meta-analysis on the individual regression parameters, testing for group differences across the WM ROI's common for age and sex as well as for male/female ratio using a two-factor between/within factor ANOVA ($p < 0.05$).

Results

1

- significantly lower FA in the 100 group in the anterior-posterior-sagittal fascicles [Edcher's D= 1.15, $p=0.0009$] and bordering linear FA in the tapetum.

11

- Increasing higher NCD in the oscillator thermic radiation and electrons in the RHE group

23

- significantly higher RDI in the R+ group in the anterior borderzone higher RDI in the superior mesio-ventral region
 - significantly higher RDI in the R+ group in the posterior borderzone

REFERENCES

This meta-analysis of pre-existing data revealed decreased FA and increased MD across multiple studies based in different countries and involving participants from different ethnicities with exposure to RME. Results aligns well with previously published reports from independent studies. Decreased FA and increased MD in the white matter regions, as a non-invasive biomarker for visual impairment in children.

Answers

Future work will include a larger sample to further examine the location and extent of white matter lesions following RHI and their associations with cognitive function. Further, we will explore the effect of sex for the location, size, age, and severity of white matter lesions.

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Figure 2. Average d' measures. Latentwise, HR, and π tests with LatentGAM's D statistics are shown* across 500s, with bars indicating 95% C.I. * Denotes significant, **Denotes p < 0.01, and * denotes p < 0.05.

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Discussion

- ▶ MOU
- ▶ Harmonizing outcome scales
- ▶ Secondary proposals
- ▶ Grant possibilities
- ▶ Workflows for new modalities

Harmonizing outcome scales

- ▶ Common test data across cohorts
- ▶ Common domains; use or create standard scores to compare
 - ▶ Working memory
 - ▶ Memory
 - ▶ Processing speed
 - ▶ Executive function
- ▶ Set impairment threshold, use categorical grouping
- ▶ Other approaches?

CHALLENGES/ OPPORTUNITIES

- *Speak the same language*
 - Defend the clinical phenotype
- Stay focused on the **Science**, not the politics/economics
- View this as PH issue, as well as pt. issue
- Prospective, longitudinal trials
 - Consider confounding B-P-S factors Type 1 and 2 error
- Emerging science

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QUESTIONS/COMMENTS

- Thank you for your time and attention!!
- Enjoy OMED

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